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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,305	01/14/2005	Toru Ishibashi	1232-5579	9351

27123 7590 04/04/2008

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EXAMINER	
BHAT, NARAYAN KAMESHWAR	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
04/04/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/521,305	ISHIBASHI ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-24* is/are rejected.

7)☒ Claim(s) *14 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 11, 2008 has been entered.

Status of the Claims

2. This action is in response to papers filed on January 11, 2008 in which claims 14 and 24 were amended. All of the amendments have been thoroughly reviewed and entered.

3. The previous rejections under 35 USC § 102 (b) and 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

4. Claims 1-24 are pending in this application.

5. Claims 14 -24 are under prosecution.

Claim Objections

6. Claims 14 and 24 are objected to because of the following informalities: The word "mercapt" in lines 12 and 13, has a typographical error. It is suggested that the

word "mercapto" be used to make the claim recitation clearer. Appropriate correction is required.

7. Claims 14 and 24 are objected to because of the following informalities: The phrase "second function group" in line 12, be rephrased to include "second functional group" to be consistent with the first functional group. Appropriate correction is required.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following are new rejections necessitated by amendments.

7. Claims 14-17 and 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chrisey et al (USPN 5,688,642 issued November 18, 1997) in view of Iwaki et al (USPGPUB NO. 2002/0039742 published Apr. 4, 2002) and further evidenced by Meisenburg et al (USPGPUB NO 2002/0198314 published Dec. 26, 2002).

Regarding claim 14, Chrisey et al teaches a method of immobilizing a probe to a solid phase carrier that include providing a DNA oligomer having thiol group, i.e., mercapto group (Fig. 3, See top panel- DNA oligomer with –SH group, Chrisey et al also refers to DNA oligomers as nucleic acid molecules, i.e., NAMs) and further teaches that DNA oligomers have a C3-C6 spacer molecules, i.e., linker molecule (column 9, lines 54-61) thus teaching a probe having a linker containing –SH group. The –SH group of Chrisey et al is the first functional group of the instant claim.

Chrisey et al further teaches providing a silica substrate with an amino silane coating (Fig. 4, immobilized silane with amino group # 42, column 6, lines 45-47), thus teaching an immobilization substrate having an amino-functional group. The amino functional group of Chrisey et al is the second functional group of the instant claim.

Chrisey et al also teaches explicitly that the substrate (Fig. 4, # 10) having an immobilized silane on the substrate (Fig. 4, # 42) binds to a DNA oligomer (Fig. 4, DNA oligomer-element # 48; left bottom panel, column 6, lines 45-54) thus teaching imparting the probe to the immobilization substrate. Chrisey et al teaches that the DNA oligomer electrostatically binds to the aminosilane coating and not to the exposed surface, which do not contain amino group (Fig. 4, see both left and right side panel, DNA binding to

only to amino group of silane and not to perfluoro alkyl group, column 6, lines 50-63, Table 1), thus teaching binding of first functional group of the probe and the second functional group of the immobilization substrate to each other.

The mercapto and the amino group taught by Chrisey et al are also the acidic and basic functional group as defined in the instant specification (see instant specification, USPGPUB, paragraph 0036). Teachings of Chrisey et al of electrostatic binding, i.e., ionic interactions of DNA oligomer having the first functional group and the substrate having second functional group also encompass first functional group and second functional group in the state of coupling without covalent binding.

As described previously, Chrisey et al teaches the electrostatic interaction between the DNA oligomer and the substrate having second functional positively charged amino group (Fig. 4, column 13, lines 13-17), but is silent about direct bonding between DNA with mercapto group and amino group via ionic bond.

Regarding claims 15 and 23, Chrisey et al teaches first functional group, i.e., mercapto group and the second functional group, i.e., an amino group. These are acidic and basic groups as defined in the instant specification (see instant specification, USPGPUB paragraph 0036). The dissociation constant of amino group is 1.0×10^{-6} (See the instant specification, Paragraph 0025) and the mercapto group is 1.0×10^{-12} or more and the dissociation constants are inherent properties of the functional groups that are chosen and both the groups of the instant claim are taught by Chrisey et al. Furthermore when the thiol group or the amino group binds to each other, causes a

change in the properties that are specific to the " thiol and amino groups" including the mutual chemical shift of signals in the NMR spectrum.

Regarding claims 16 and 17, Chrisey et al teaches that probe comprises of a DNA oligomer (Fig. 1, element # 19) and the spacer, i.e., linker is between the DNA and the thiol group (column 9, lines 54-61) which is at the 3' terminal end (Fig. 3, top panel; see the –thiol group at the 3' end of the DNA oligomer), thus linker is at the 3' end.

Regarding claims 19 and 20, as described previously, Chrisey et al teaches the mercapto group as the first functional group and the primary amino group (-NH2 group) as the second functional group (Fig. 4) and are the acidic and basic functional groups.

Regarding claim 21, Chrisey et al teaches that the second functional group is introduced by treatment of the solid phase carrier with an aminosilane coupling agent (Fig. 4, # 42, column 6, lines 46-47).

Regarding claim 22, Chrisey et al teaches the substrate is the glass (column 7, lines 24-33), which is a solid phase carrier of the instant claim.

Regarding claim 24, Chrisey et al teaches a method of immobilizing a probe to a solid phase carrier that include providing DNA oligomers having thiol group, i.e., mercapto group (column 8, lines 41-67, Chrisey et al also refers to DNA oligomers as nucleic acid molecules, i.e., NAMs) and further teaches that DNA oligomers have a C3-C6 spacer molecules, i.e., linker molecule (column 9, lines 54-61) thus teaching a plurality of probes each having a linker containing –SH group. The –SH group of Chrisey et al is the first functional group of the said claim.

Chrisey et al further teaches providing a silica substrate coated with aminosilane on at least two different regions separated by a region not having aminosilane with primary amino groups exposed on the substrate (Fig. 4, # 42, column 6, lines 45-47), thus teaching an immobilization substrate having a plurality of amino functional group. The amino functional groups of Chrisey et al are the pluralities of the second functional group of the instant claim.

Chrisey et al also explicitly teaches that the substrate (column 6, lines 46-47) having an aminosilane coating at multiple locations (Fig. 4, element # 42) binds electrostatically with DNA oligomers (Fig. 4, DNA oligomer-element # 48; left bottom panel, column 6, lines 45-54) thus teaching imparting the probe to the immobilization substrate. Chrisey et al further teaches that the DNA oligomer binds to the aminosilane coating and not to the exposed surface, which do not contain amino group (Fig. 4, see both left and right side panel, DNA electrostatically binding to only to amino group of silane and not to perfluoro alkyl group, column 6, lines 50-63, Table 1), thus teaching binding of first functional group of the probe and the second functional group of the immobilization substrate to each other.

The mercapto and the amino group taught by Chrisey et al are also the acidic and basic functional group as defined in the instant specification (see instant specification, USPGPUB, paragraph 0036). Teachings of Chrisey et al of electrostatic binding, i.e., ionic interactions of DNA oligomer having the first functional group and the substrate having second functional group also encompass first functional group and second functional group in the state of coupling without covalent binding.

As described previously, Chrisey et al teaches explicitly the electrostatic interaction between DNA oligomer and the substrate having second functional positively charged amino group (Fig. 4, column 13, lines 13-17).

Regarding claims 14 and 24, Chrisey et al is silent about direct bonding between DNA with mercapto group and amino group via ionic bond. However, direct bonding between mercapto group and amino group via ionic bond was known in the art before the claimed invention was made as taught by Iwaki et al who teaches explicitly immobilization of probe molecules on solid phase carrier by electrostatic binding (Examples 4-6, paragraphs 0097-0102). Iwaki et al also teaches that the surface of solid phase carrier has the amino group and the DNA oligonucleotides have the mercapto group (paragraph 0008). Iwaki et al further teaches that solid phase carrier is coated with aminosilane and contacted with DNA molecules carrying appropriate anionic groups forms an electrostatic binding, i.e., ionic bond between the solid phase carrier and the DNA molecules (paragraph 0057).

The mercapto group is known in the art as an anionic group, which is further substantiated by Meisenburg et al (paragraph 0141). It is noted that the reference of Meisenburg et al is only used to further support of the fact known in the art that –SH groups are anionic. Iwaki et al thus teaches the ionic bond formed between anionic groups on the DNA molecules including mercapto groups and the amino groups on the surface of the solid phase carrier. Thus Chrisey et al in view of Iwaki et al teaches method steps recited in claims 14 and 24.

Iwaki et al also teaches that even the charge neutral PNA molecules are fixed to the substrate with incorporation of the appropriate anionic groups and fixing DNA oligomers on to the substrate via electrostatic bonding is simple and produces low coefficient of variation in hybridization assays (Examples 4-6, Table 2, paragraphs 0057, 0097-0102).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to include electrostatic bonding of DNA and PNA oligomers with appropriate anionic groups on the substrate with the expected benefit of fixing charge neutral PNA molecules on to the substrate, which produces low coefficient of variation in hybridization assays as taught by Iwaki et al (Examples 4-6, Table 2, paragraphs 0057, 0097-0102).

8. Claims 14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chrisey et al (USPN 5,688,642 issued November 18, 1997) in view of Iwaki et al (USPGPUB NO. 2002/0039742 published Apr. 4, 2002) as applied to claim 14 above, and further in view of McGovern et al (USPN 6,159,695 issued December 12, 2000).

Claim 18 is dependent on claim 14. Teachings of Chrisey et al and Iwaki et al regarding the claim 14 are described previously in this office action on pages 4-5 and 8.

Regarding claim 18, Chrisey et al teaches immobilizing probe linker contains spacer molecules of C3-C6 (column 9, lines 54-61). Chrisey et al do not teach the linker comprises a polyether chain. McGovern et al teaches attachment of tether linker to oligonucleotides (Fig. 4) with polyether linker of 2-50 unit (Column 22, lines 53 –58).

McGovern et al also teaches tether linker supply the oligonucleotide with reactive functionality so that it can be chemically manipulated, and to allow the oligonucleotide to extend any specified distance away from the surface (column 7, lines 18-22).

It would be obvious to one having the ordinary skill in the art at the time the invention was made to use the oligonucleotide with tether linker with polyether chain as taught by McGovern et al as alternatives to the C3-C6 linker containing DNA oligomer of Chrisey et al and Iwaki et al. One would be motivated to do so to provide additional equivalent probes and also with the expected benefit of providing additional reactive functionality so that probe can be chemically manipulated, thus allowing the oligonucleotide to extend any specified distance away from the surface as taught by McGovern et al (Column 7, lines 18-22) thus improving the probe immobilization method of Chrisey et al in view of Iwaki et al.

Response to Remarks from the applicants

Claim Rejections under 35 U.S.C. § 102(b)

9. Applicant's arguments with respect to claims 14 and 24, filed on December 3, 2007 have been fully considered but are moot in view of the new grounds of rejection necessitated by claim amendments.

Applicant has acknowledged that Chrisey et al is interested in the electrostatic bonding of DNA oligomers to the aminosilane coupling agent on the substrate (Remarks, pg. 8, last paragraph, Chrisey et al, Fig. 4, and Examples 3-5). Chrisey et al also teaches that the DNA oligomers immobilized via electrostatic means on an

organosilane SAM is able to hybridize with complementary partner but not with a mismatched partner and able to withstand hybridization and washing steps, thus teaching bonding of DNA oligomer to the substrate is strong (Example 3).

The only difference between the instant invention and the invention of Chrisey et al is that, Chrisey et al is silent about direct bonding between DNA with mercapto group and amino group via ionic bond. However, as described in detail in this office action, Iwaki et al teaches the electrostatic bonding between mercapto group and the amino group (Office action, pgs. 8-9). Since teachings of Chrisey et al in view of Iwaki et al teaches all the limitation of the claimed invention, Applicant's arguments are not persuasive.

Claim Rejections under 35 U.S.C. § 103(a)

10. Applicant's arguments with respect to claim 18 have been considered but are moot in view of the new grounds of rejection necessitated by claim amendments.

Since Chrisey et al in view of Iwaki et al teaches all the limitation of claim 14, and as described in detail in this office action, McGovern et al teaches the polyether linker (Fig. 4, column 22, lines 53 –58, limitation of claim 18) and combined teachings of Chrisey et al, Iwaki et al and McGovern et al teaches all the limitation of claim 18 (this office action, pgs. 9-10), Applicant's arguments are not persuasive.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on (571)-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Narayan K. Bhat/

Examiner, Art Unit 1634

Narayan K. Bhat, Ph. D.

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